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Docket No. 0776/1F216-US2

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Allan **SVENDSEN**, *et al.*

Serial No.: 09/327,563 Group Art Unit: 1652

Filed: June 8, 1999 Examiner: E. Slobodansky

For: **α-AMYLASE MUTANTS**

- -

June 2, 2000

Director of Patents
Washington, D.C. 20231

REQUEST PURSUANT TO 37 C.F.R. §1.607 FOR INTERFERENCE WITH U.S. PATENT NO. 5,763,385

Sir:

Applicants hereby request, pursuant to 37 C.F.R. §1.607, that an interference be declared between the above-identified application and U.S. Patent No. 5,763,385.

I. Identification Pursuant to 37 C.F.R. §1.607(a)(1) of Patent

Applicants request that an interference be declared between the above-identified application and U.S. Patent No. 5,763,385 of Richard R. Bott and Andrew Shaw, entitled "Modified α-Amylases Having Altered Calcium Binding Properties" (the '385 patent"). The '385 patent issued on June 9, 1998, less than one year before claims were filed in the present application which are the same as or for the same or substantially the same subject matter as a claim or claims of the '385 patent. The '385 patent is assigned to Genencor International, Inc., Rochester, New York. A copy of the '385 patent is attached hereto as Exhibit 1.

II. Presentation of a Proposed Count

Applicants propose the following count as the count of the requested interference.

Count

A variant of a parent alpha-amylase, said variant having an amino acid sequence which differs from the amino acid sequence of said parent, wherein the difference between said variant and said parent comprises a different amino acid residue in said variant than in said parent at one or more positions selected from the group consisting of the positions which correspond to amino acid residues Q298, G299, G301, Y302, L307, N309, Q340, F343, F403, H405, H406, D407, G410, L427, I428, D430, D433, K436, N473, G474, and G475 in *Bacillus licheniformis* alpha-amylase.

III. Identification Pursuant to 37 C.F.R. §1.607(a)(3) of Claims of the '385 Patent Corresponding to the Proposed Count

The '385 patent includes 28 claims. All of the claims of the '385 patent correspond to the proposed Count. All of the claims of the '385 patent are directed to embodiments of a single invention, variant alpha-amylases which are modified at one or more particular amino acid position(s), and detergents and starch liquefaction compositions comprising these alpha-amylases.

IV. Identification Pursuant to 37 C.F.R. §1.607(4) of Claims in the Present Application which Correspond to the Proposed Count

Claims 77-81, 84-88, ~~90-93~~ 90-92, 97, 113~~-187~~ 120, and 192~~-213~~ 206, 208-213, of which claims 193-213 are added to the present application in the Supplemental Preliminary Amendment filed concurrently herewith, correspond to the proposed Count (a copy of the Supplemental Preliminary Amendment is attached hereto as Exhibit 2).

The proposed Count defines substantially the same invention as that claimed in claims 77-81, 84-88, 90-93, 97, 113-187, and 192-213. Although these claims include several limitations which do not appear in the proposed Count or specify only one of the amino acid positions of the proposed Count, these claims are directed to embodiments of a single invention - a variant alpha-amylase which differs from a parent alpha-amylase at one or more of the amino acid positions specified in the proposed Count.

Therefore, applicants submit that there is interfering subject matter between claims 1-28 of the '385 patent and pending claims 77-81, 84-88, 90-93, 97, 113-187, and 192-213 of the present application. Accordingly, applicants request that an interference be declared under 37 C.F.R. §1.611, having the Count and the corresponding claims as proposed above.

V. Explanation Pursuant to 37 C.F.R. §1.607(a)(4) of Why Each Claim of the '385 Patent That Does Not Correspond Exactly to the Proposed Count Corresponds to the Proposed Count

Applicants submit that the claims of the '385 patent include several limitations which describe latent properties of alpha-amylases or properties which are not necessary to describe the claimed invention. Accordingly, applicants have presented a Count with one or more of these latent properties omitted from the Count or with these immaterial limitations omitted.[1]

Claim 1 of the '385 Patent

Claim 1 of the '385 patent corresponds substantially to the proposed Count. The proposed Count calls for a variant of a parent alpha-amylase. Claim 1 of the '385 patent calls for an alpha-amylase which is modified. An alpha-amylase which is modified is a type of variant alpha-amylase. The '385 patent specification clearly explains that the claimed invention is directed to a variant that is prepared from a parent alpha-amylase. For example:

> Residues in α-amylase are identified herein for deletion or substitution. Thus, specific residues discussed herein refer to an amino acid position number which references the number assigned to the mature *Bacillus licheniformis* α-amylase sequence illustrated in FIG. 4. The invention, however, is not limited to the mutation of the particular mature α-amylase of *Bacillus licheniformis* but extends to non-*Bacillus licheniformis* precursor α-amylases containing amino acid residues at positions which are equivalent to the particular identified residue in *Bacillus licheniformis* α-amylase. A residue of a precursor

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[1] Recitation of a latent or new property of the claimed invention does not define a patentable invention. *See, e.g., Harris Corp. v. EXYS Corp.*, 114 F.3d 1149, 1153 (Fed. Cir. 1997). *See also In re Spada*, 911 F.2d 705, 708 (Fed. Cir. 1990), *Titanium Metals Corp. of Am. v. Banner*, 778 F.2d 775, 781-82 (Fed. Cir. 1985).

> α-amylase is equivalent to a residue of *Bacillus licheniformis* α-amylase if it is either homologous (i.e., corresponds in position for either the primary or tertiary structure) or analogous to a specific residue or portion of that residue in *Bacillus licheniformis* α-amylase (i.e., having the same or similar functional capacity to combine, react, or interact chemically or structurally). [Exh. 1, 8:47-63]

Therefore, the term "variant of a parent alpha-amylase" of the proposed Count describes the alpha-amylases of claim 1 of the '385 patent.

Claim 1 specifies that the alpha-amylase includes an A domain, a C domain, and a calcium binding site which is associated with the A and C domains.[2] The '385 patent specification explains that these are major structural elements common to alpha-amylases. For example, the '385 patent states that:

> α-amylases from different organisms have been shown to exhibit similar three-dimensional structure despite considerable differences in primary structure. FIG. 1 illustrates the structure of α-amylase of *Bacillus licheniformis*. While some inter-species variation will exist between the various α-amylases. It is believed that the major structural elements of *Bacillus licheniformis* α-amylase are representative of α-amylase structures in general (see Brayer et al., Protein Sci., vol. 4, pp. 1730-1742 (1995); Larson et al., J. Mol. Biol. vol. 235, pp. 1560-1584 (1994); Qian et al., J. Mol. Biol. vol. 231, pp. 785-799 (1993)). [Exh. 1, 2:32-42].
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> Three dimensional structure similarities between various α-amylases (and related amylolytic enzymes like cyclodextrin glycosyltransferases and α-glucosidases) from different organisms,

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[2] There is a typographical error in claim 1. The word "and" should be inserted so that claim 1 reads as follows:

> An α-amylase comprising an A domain, a C domain and a calcium binding site, wherein said calcium binding site is associated with said A domain and said C domain ***and*** comprises .... *See* Exh. 1, 5:8-12.

despite differences in their primary structure, are found in the common presence of an α/β-barrel forming a central part (domain A), a Greek key motif as a separate domain C and at least one additional domain, domain B (Machius et al., supra). Substrate binding is believed to be localized to a cleft between the α/β-barrel and domain B, comprising several β strands of variable length, depending on the species (Machius, supra). Also common is a requirement for calcium which is believed to maintain structural integrity. [Exh. 1, 3:10-22].

* * * *

The major structural elements, including the newly discovered CalB site which is disclosed herein, and changes thereto to alter the performance of an α-amylase are described below in general terms as applicable to most α-amylases. As shown in FIG. 1, three major domains are defined, the A domain, the B domain and the C domain as well as two calcium binding sites, CalA and CalB. The A domain comprises the central portion of the molecule and has been identified as an α/β or TIM barrel. The α/β barrel is made of a series of parallel β-strands which are interconnected by α-helices. On the carboxyl end of the enzymes on one side of the A domain is a region comprising an anti-parallel β-barrel known as a "Greek key" motif (see, e.g., Richardson et al., Advan. Protein Chem. vol. 34, 167-339 (1981); Braden et al., Introduction to Protein Structure, Garland Publishing Inc., New York (1991)). This domain has been identified as the C domain. On the opposite side of the A domain from the C domain (the N-terminal) is an additional domain which comprises several β strands of variable length depending on the species, known as the B domain. The B domain has been recognized as being highly variable between α-amylases of different species and often comprises extended loops. It is believed that substrate binding is localized to a cleft between the A domain and the B domain and that the active site is further associated with this region of the molecule. The CalA binding site is located within a cleft separating the A domain and the B domain and is believed to provide stability to this region. The CalB binding site disclosed herein is located in the region where the A domain and the C domain interface. [Exh. 1, 8:5-34].

* * * *

The segments of the α-amylase polypeptide chain which comprise the CalB binding site include residues 290-309, 339-347, 402-411, 426-436 and 472-477. [Exh. 1, 9:42-44].

It is clear from the '385 patent specification that alpha-amylases generally include a calcium binding site associated with the A and C domains. This is simply a latent property of alpha-amylases, and it is not necessary to recite this limitation in the proposed Count.[3]

Claim 1 of the '385 patent also specifies that the calcium binding site include ligands in the A and/or C domains.[4] The '385 patent specification explains that alpha-amylases in general are similar. Therefore, alpha-amylases latently include ligands in the A and/or C domains.

> Three dimensional structure similarities between various α-amylases (and related amylolytic enzymes like cyclodextrin glycosyltransferases and α-glucosidases) from different organisms, despite differences in their primary structure, are found in the common presence of an α/β-barrel forming a central part (domain A), a Greek key motif as a separate domain C and at least one additional domain, domain B (Machius et al., supra). [Exh. 1, 3:10-17].
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> * * * *
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> Also common is a requirement for calcium which is believed to maintain structural integrity. [Exh. 1, 3:20-22].
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> * * * *
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> With respect to the calcium binding site within α-amylase discovered by Applicants, five amino acid ligands have been identified which are believed to act as calcium ligands. The calcium ligands residues comprise amino acid residues equivalent to G300, Y302, H406, D407 and D430 in *Bacillus licheniformis* α-amylase. Specifically with respect to these identified calcium ligands, the carbonyl oxygens of G300, Y302 and H406 and the side-chains of D407 and D430 are believed to be implicated in binding calcium. [Exh. 1, 6:58-67].

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[3] *See* footnote 1, above.

[4] *See* footnote 2, above.

Therefore, it is unnecessary to include this limitation in the proposed Count.[5]

Claim 1 of the '385 patent also calls for the modification to alter the characteristics of the calcium binding site and to alter the performance of the alpha-amylase. Again, the '385 patent specification clearly explains that substitutions at the positions specified in the proposed Count yield this result. The '385 patent explains that:

> The segments of the α-amylase polypeptide chain which comprise the CalB binding site include residues 290-309, 339-347, 402-411, 426-436 and 472-477. These polypeptide segments comprise the CalB binding site. Accordingly, regiospecific random mutations in these regions would be expected to yield variants that modulate the stability of α-amylase via modulation of the affinity of calcium at this site [Exh. 1, 9:42-49].

Accordingly, this limitation is a latent property of the claimed alpha-amylases, and it is unnecessary to include this limitation in the proposed Count.[6] Therefore, the proposed Count and claim 1 of the '385 patent are directed to the same patentable invention.

Claim 2 of the '385 Patent

Claim 2 depends from claim 1 and further specifies that the alpha-amylase is produced by *Bacillus*. The '385 patent specification acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that "α-Amylases are produced by a wide variety of microorganisms including Bacillus...." Exh. 1, 1:23-24.

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[5] *See* footnote 1, above.

[6] *See* footnote 1, above.

This limitation does not patentably distinguish claim 2 of the '385 patent from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 2 corresponds to the proposed Count.

Claim 3 of the '385 Patent

Claim 3 depends from claim 2 and further specifies that the alpha-amylase is produced by *B. licheniformis, B. amyloliquefaciens,* or *B. stearothermophilus*. The '385 patent acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that most commercial amylases were produced by *B. licheniformis, B. amyloliquefaciens, B. subtilis*, or *B. stearothermophilus*. Exh. 1, 1:25-28.

This limitation does not patentably distinguish claim 3 of the '385 patent from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 3 corresponds to the proposed Count.

Claim 4 of the '385 Patent

Claim 4 depends from claim 1 and further specifies a detergent which comprises the alpha-amylase of claim 1. The '385 patent specification, in the "BACKGROUND OF THE INVENTION" cites PCT Publication No. WO95/10603 as disclosing *B. licheniformis* alpha-amylase variants which have improved laundry or dishwashing performance. Exh. 1, 1:47-52. The '385 patent further states, in the BACKGROUND OF THE INVENTION, that:

> α-Amylases are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile

> industry for starch desizing, α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 4 of the '385 patent from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 4 corresponds to the proposed Count.

Claim 5 of the '385 Patent

Claim 5 depends from claim 1 and further specifies a starch liquefaction composition which comprises the alpha-amylase of claim 1. The '385 patent specification, in the "BACK-GROUND OF THE INVENTION", cites PCT Publication No. WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the specific substitutions Ala-111-Thr, His-133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

Again, the '385 patent further states that:

> α-Amylase are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing. α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 5 of this '385 patent from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 5 corresponds to the proposed Count.

Claim 6 of the '385 Patent

Claim 6 depends from claim 1 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, V128, H133, W138, N188, A209 and/or M197 in *B. licheniformis*. The '385 patent specification cites and describes PCT Publication No. WO95/10603 as follows:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52]

and WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the specific substitutions Ala-111-Thr, His, 133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

This limitation does not patentably distinguish claim 6 of the '385 patent from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 6 corresponds to the proposed Count.

Claim 7 of the '385 Patent

Claim 7 depends from claim 1 and further specifies that the alpha-amylase is modified by substituting an amino acid at a position corresponding to one or more of G301, H405, H406 and/or K436 in *B. licheniformis*. These amino acid positions are members of the group of amino acid positions specified in claim 1 of the '385 patent. For the reasons explained above with respect to claim 1, claim 7 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 7 of the '385 patent are directed to the same patentable invention.

Claim 8 of the '385 Patent

Claim 8 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is Q298 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 8 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 8 of the '385 patent are directed to the same patentable invention.

Claim 9 of the '385 Patent

Claim 9 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is G299 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 9 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 9 of the '385 patent are directed to the same patentable invention.

Claim 10 of the '385 Patent

Claim 10 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is G301 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 10 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 10 of the '385 patent are directed to the same patentable invention.

Claim 11 of the '385 Patent

Claim 11 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is Y302 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 11 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 11 of the '385 patent are directed to the same patentable invention.

Claim 12 of the '385 Patent

Claim 12 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is L307 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 12 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 12 of the '385 patent are directed to the same patentable invention.

Claim 13 of the '385 Patent

Claim 13 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is N309 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 13 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 13 of the '385 patent are directed to the same patentable invention.

Claim 14 of the '385 Patent

Claim 14 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is Q340 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 14 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 14 of the '385 patent are directed to the same patentable invention.

Claim 15 of the '385 Patent

Claim 15 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is F343 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 15 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 15 of the '385 patent are directed to the same patentable invention.

Claim 16 of the '385 Patent

Claim 16 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is F403 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 16 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 16 of the '385 patent are directed to the same patentable invention.

Claim 17 of the '385 Patent

Claim 17 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is H405 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 17 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 17 of the '385 patent are directed to the same patentable invention.

Claim 18 of the '385 Patent

Claim 18 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is H406 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 18 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 18 of the '385 patent are directed to the same patentable invention.

Claim 19 of the '385 Patent

Claim 19 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is D407 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 19 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 19 of the '385 patent are directed to the same patentable invention.

Claim 20 of the '385 Patent

Claim 20 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is G410 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 20 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 20 of the '385 patent are directed to the same patentable invention.

Claim 21 of the '385 Patent

Claim 21 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is L427 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 21 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 21 of the '385 patent are directed to the same patentable invention.

Claim 22 of the '385 Patent

Claim 22 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is I428 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 22 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 22 of the '385 patent are directed to the same patentable invention.

Claim 23 of the '385 Patent

Claim 23 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is D430 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 23 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 23 of the '385 patent are directed to the same patentable invention.

Claim 24 of the '385 Patent

Claim 24 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is G433 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 24 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 24 of the '385 patent are directed to the same patentable invention.

Claim 25 of the '385 Patent

Claim 25 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is K436 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 25 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 25 of the '385 patent are directed to the same patentable invention.

Claim 26 of the '385 Patent

Claim 26 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is N473 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 26 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 26 of the '385 patent are directed to the same patentable invention.

Claim 27 of the '385 Patent

Claim 27 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is G474 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 27 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 27 of the '385 patent are directed to the same patentable invention.

Claim 28 of the '385 Patent

Claim 28 of the '385 patent is an independent claim which is identical to claim 1, except that the only amino acid position specified is G475 in *B. licheniformis*. For the reasons explained above with respect to claim 1, claim 28 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 28 of the '385 patent are directed to the same patentable invention.

VI. Explanation Pursuant to 37 C.F.R. §1.607(a)(4) of Why Each Claim of the Present Application That Does Not Correspond Exactly to the Proposed Count, Corresponds to the Proposed Count

Claim 77 of the Present Application

Claim 77 of the present application corresponds substantially to the proposed Count. The proposed Count calls for a variant of a parent alpha-amylase. Claim 77 of the present application calls for an alpha-amylase which is modified. An alpha-amylase which is modified is a type of variant alpha-amylase. Therefore, the term "variant of a parent alpha-amylase" of the proposed Count describes the alpha-amylases of claim 77 of the present application.

Claim 77 specifies that the alpha-amylase includes an A domain, a C domain, and a calcium binding site which is associated with the A and C domains.[7] The '385 patent specification explains that these are major structural elements common to alpha-amylases. For example, the '385 patent states that:

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[7] Claim 77 of the present application contains the same typographical error as does claim 1 of the '385 patent. *See* footnote 2, above.

α-amylases from different organisms have been shown to exhibit similar three-dimensional structure despite considerable differences in primary structure. FIG. 1 illustrates the structure of α-amylase of *Bacillus licheniformis*. While some inter-species variation will exist between the various α-amylases. It is believed that the major structural elements of *Bacillus licheniformis* α-amylase are representative of α-amylase structures in general (see Brayer et al., Protein Sci., vol. 4, pp. 1730-1742 (1995); Larson et al., J. Mol. Biol. vol. 235, pp. 1560-1584 (1994); Qian et al., J. Mol. Biol. vol. 231, pp. 785-799 (1993)). [Exh. 1, 2:32-42].

* * * *

Three dimensional structure similarities between various α-amylases (and related amylolytic enzymes like cyclodextrin glycosyltransferases and α-glucosidases) from different organisms, despite differences in their primary structure, are found in the common presence of an α/β-barrel forming a central part (domain A), a Greek key motif as a separate domain C and at lest one additional domain, domain B (Machius et al., supra). Substrate binding is believed to be localized to a cleft between the α/β-barrel and domain B, comprising several β strands of variable length, depending on the species (Machius, supra). Also common is a requirement for calcium which is believed to maintain structural integrity. [Exh. 1, 3:10-22].

* * * *

The major structural elements, including the newly discovered CalB site which is disclosed herein, and changes thereto to alter the performance of an α-amylase are described below in general terms as applicable to most α-amylases. As shown in FIG. 1, three major domains are defined, the A domain, the B domain and the C domain as well as two calcium binding sites, CalA and CalB. The A domain comprises the central portion of the molecule and has been identified as an α/β or TIM barrel. The α/β barrel is made of a series of parallel β-strands which are interconnected by α-helices. On the carboxyl end of the enzymes on one side of the A domain is a region comprising an anti-parallel β-barrel known as a "Greek key" motif (see, e.g., Richardson et al., Advan. Protein Chem. vol. 34, 167-339 (1981); Braden et al., Introduction to Protein Structure, Garland Publishing Inc., New York (1991)). This domain has been identified as the C domain. On the opposite side of the A domain from the C domain (the N-terminal) is an additional domain which comprises several β

strands of variable length depending on the species, known as the B domain. The B domain has been recognized as being highly variable between α-amylase of different species and often comprises extended loops. It is believed that substrate binding is localized to a cleft between the A domain and the B domain and that the active site is further associated with this region of the molecule. The CalA binding site is located within a cleft separating the A domain and the B domain and is believed to provide stability to this region. The CalB binding site disclosed herein is located in the region where the A domain and the C domain interface. [Exh. 1, 8:5-34].

* * * *

The segments of the α-amylase polypeptide chain which comprise the CalB binding site include residues 290-309, 339-347, 402-411, 426-436 and 472-477. [Exh. 1, 9:42-44].

It is clear from the '385 patent specification that alpha-amylases generally include a calcium binding site associated with the A and C domains. This is simply a latent property of alpha-amylases and is not necessary to recite this limitation in the proposed Count.[8]

Claim 77 of the present application also specifies that the calcium binding site include ligands in the A and/or C domains. The '385 patent specification explains that alpha-amylases in general are similar. Therefore, alpha-amylases latently include ligands in the A and/or C domains.

Three dimensional structure similarities between various α-amylases (and related amylolytic enzymes like cyclodextrin glycosyltransferases and α-glucosidases) from different organisms, despite differences in their primary structure, are found in the common presence of an α/β-barrel forming a central part (domain A), a Greek key motif as a separate domain C and at least one additional domain, domain B (Machius et al., supra). [Exh. 1, 3:10-17].

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[8] *See* footnote 1, above.

> Also common is a requirement for calcium which is believed to maintain structural integrity. [Exh. 1, 3:20-22].
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> With respect to the calcium binding site within α-amylase discovered by Applicants, five amino acid ligands have been identified which are believed to act as calcium ligands. The calcium ligands residues comprise amino acid residues equivalent to G300, Y302, H406, D407 and D430 in *Bacillus licheniformis* α-amylase. Specifically with respect to these identified calcium ligands, the carbonyl oxygens of G300, Y302 and H406 and the side-chains of D407 and D430 are believed to be implicated in binding calcium. [Exh. 1, 6:58-67].

Therefore, it is unnecessary to include this limitation in the proposed Count.[9]

Claim 77 of the present application also calls for the modification to alter the characteristics of the calcium binding site and to alter the performance of the alpha-amylase. Again, the '385 patent specification clearly explains that substitutions at the positions specified in the proposed Count yield this result. The '385 patent explains that:

> The segments of the α-amylase polypeptide chain which comprise the CalB binding site include residues 290-309, 339-347, 402-411, 426-436 and 472-477. These polypeptide segments comprise the CalB binding site. Accordingly, regiospecific random mutations in these regions would be expected to yield variants that modulate the stability of α-amylase via modulation of the affinity of calcium at this site [Eh. 1, 9:42-49].

Accordingly, this limitation is a latent property of the claimed alpha-amylases, and it is unnecessary to include this limitation in the proposed Count.[10]

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[9] *See* footnote 1, above.

[10] *See* footnote 1, above.

Claim 77 of the present application specifies an amino acid position specified is in the proposed Count, Q298 in *B. licheniformis*.

Therefore, the proposed Count and claim 77 of the '385 patent are directed to the same patentable invention.

Claim 78 of the Present Application

Claim 78 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is G299 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 78 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 78 of the present application are directed to the same patentable invention.

Claim 79 of the Present Application

Claim 79 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is G301 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 79 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 79 of the present application are directed to the same patentable invention.

Claim 80 of the Present Application

Claim 80 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is Y302 in *B. licheniformis*. For the reasons

explained above with respect to claim 77, claim 80 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 80 of the present application are directed to the same patentable invention.

Claim 81 of the Present Application

Claim 81 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is L307 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 81 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 81 of the present application are directed to the same patentable invention.

Claim 84 of the Present Application

Claim 84 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is F343 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 84 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 84 of the present application are directed to the same patentable invention.

Claim 85 of the Present Application

Claim 85 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is F403 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 85 corresponds substantially to the proposed Count.

Therefore, both the proposed Count and claim 85 of the present application are directed to the same patentable invention.

Claim 86 of the Present Application

Claim 86 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is H405 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 86 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 86 of the present application are directed to the same patentable invention.

Claim 87 of the Present Application

Claim 87 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is H406 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 87 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 87 of the present application are directed to the same patentable invention.

Claim 88 of the Present Application

Claim 88 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is D407 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 88 corresponds substantially to the proposed Count.

Therefore, both the proposed Count and claim 88 of the present application are directed to the same patentable invention.

Claim 90 of the Present Application

Claim 90 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is L427 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 90 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 90 of the present application are directed to the same patentable invention.

Claim 91 of the Present Application

Claim 91 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is L428 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 91 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 91 of the present application are directed to the same patentable invention.

Claim 92 of the Present Application

Claim 92 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is D430 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 92 corresponds substantially to the proposed Count.

Therefore, both the proposed Count and claim 92 of the present application are directed to the same patentable invention.

Claim 93 of the Present Application

Claim 93 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is G433 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 93 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 93 of the present application are directed to the same patentable invention.

Claim 97 of the Present Application

Claim 97 of the present application is an independent claim which is identical to claim 77, except that the amino acid position specified is G475 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 97 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 97 of the present application are directed to the same patentable invention.

Claim 113 of the Present Application

Claim 113 of the present application is an independent claim which is identical to claim 77, except that the amino acid positions specified are Q298, G299, G301, Y302, L307, F343, F403, H405, H406, D407, L427, I428, D430, G433, and G475 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 113 corresponds substantially to the proposed

Count. Therefore, both the proposed Count and claim 113 of the present application are directed to the same patentable invention.

Claim 114 of the Present Application

Claim 114 depends from claim 113 and further specifies that the alpha-amylase is produced by *Bacillus*. The '385 patent specification acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that "α-Amylases are produced by a wide variety of microorganisms including Bacillus...." Exh. 1, 1:23-24.

This limitation does not patentably distinguish claim 114 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 114 corresponds to the proposed Count.

Claim 115 of the Present Application

Claim 115 depends from claim 114 and further specifies that the alpha-amylase is produced by *B. licheniformis, B. amyloliquefaciens,* or *B. stearothermophilus*. The '385 patent acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that most commercial amylases were produced by *B. licheniformis, B. amyloliquefaciens, B. subtilis*, or *B. stearothermophilus*. Exh. 1, 1:25-28.

This limitation does not patentably distinguish claim 115 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 115 corresponds to the proposed Count.

Claim 116 of the Present Application

Claim 116 depends from claim 113 and further specifies a detergent which comprises the alpha-amylase of claim 113. The '385 patent specification, in the "BACKGROUND OF THE INVENTION" cites PCT Publication No. WO94/10603 as disclosing *B. licheniformis* alpha-amylase variants which have improved laundry or dishwashing performance. Exh. 1, 1:47-52. The '385 patent further states, in the BACKGROUND OF THE INVENTION, that:

> α-Amylases are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing, α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 116 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 116 corresponds to the proposed Count.

Claim 117 of the Present Application

Claim 117 depends from claim 113 and further specifies a starch liquefaction composition which comprises the alpha-amylase of claim 113. The '385 patent specification, in the "BACKGROUND OF THE INVENTION", cites PCT Publication No. WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the

specific substitutions Ala-111-Thr, His-133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

Again, the '385 patent further states that:

> α-Amylase are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing. α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 117 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 117 corresponds to the proposed Count.

Claim 118 of the '385 Patent

Claim 118 depends from claim 113 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, N188, A209 and/or M197 in *B. licheniformis*. The '385 patent specification cites and describes PCT Publication No. WO95/10603 as follows:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52].

This limitation does not patentably distinguish claim 118 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 118 corresponds to the proposed Count.

Claim 119 of the Present Application

Claim 119 depends from claim 113 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, V128, H133, N188, A209 and/or M197 in *B. licheniformis*. The '385 patent specification cites PCT Publication No. WO95/10603 as disclosing that:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52]

and WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the specific substitutions Ala-111-Thr, His, 133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

This limitation does not patentably distinguish claim 119 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 119 corresponds to the proposed Count.

Claim 120 of the Present Application

Claim 120 depends from claim 113 and further specifies that the alpha-amylase is modified by substituting an amino acid at a position corresponding to one or more of G301, H405, H406 and/or K436 in *B. licheniformis*. These amino acid positions are members of the group of amino acid positions specified in claim 113 of the present application. Therefore, the proposed Count and claim 120 of the present application are directed to the same patentable invention.

Claim 121 of the Present Application

Claim 121 of the present application is an independent claim which is identical to claim 77, except that the amino acid positions specified are Q298, G299, G301, Y302, L307, F343, H405, H406, D407, I428, D430, and G475 in *B. licheniformis*. For the reasons explained above with respect to claim 77, claim 121 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 121 of the present application are directed to the same patentable invention.

Claim 122 of the Present Application

Claim 122 depends from claim 121 and further specifies that the alpha-amylase is produced by *Bacillus*. The '385 patent specification acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that "α-Amylases are produced by a wide variety of microorganisms including Bacillus...." Exh. 1, 1:23-24.

This limitation does not patentably distinguish claim 122 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 122 corresponds to the proposed Count.

Claim 123 of the Present Application

Claim 123 depends from claim 122 and further specifies that the alpha-amylase is produced by *B. licheniformis, B. amyloliquefaciens,* or *B. stearothermophilus*. The '385 patent acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that most

commercial amylases were produced by *B. licheniformis, B. amyloliquefaciens, B. subtilis*, or *B. stearothermophilus*. Exh. 1, 1:25-28.

This limitation does not patentably distinguish claim 123 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 123 corresponds to the proposed Count.

Claim 124 of the Present Application

Claim 124 depends from claim 121 and further specifies a detergent which comprises the alpha-amylase of claim 121. The '385 patent specification, in the "BACKGROUND OF THE INVENTION" cites PCT Publication No. WO94/10603 as disclosing *B. licheniformis* alpha-amylase variants which have improved laundry or dishwashing performance. Exh. 1, 1:47-52. The '385 patent further states, in the BACKGROUND OF THE INVENTION, that:

> α-Amylases are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing, α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 124 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 124 corresponds to the proposed Count.

Claim 125 of the Present Application

Claim 125 depends from claim 121 and further specifies a starch liquefaction composition which comprises the alpha-amylase of claim 121. The '385 patent specification, in the "BACKGROUND OF THE INVENTION", cites PCT Publication No. WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the specific substitutions Ala-111-Thr, His-133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

Again, the '385 patent further states that:

> α-Amylase are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing. α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 125 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 125 corresponds to the proposed Count.

Claim 126 of the '385 Patent

Claim 126 depends from claim 121 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, N188, A209 and/or M197 in

B. licheniformis. The '385 patent specification cites and describes PCT Publication No. WO95/10603 as follows:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52].

This limitation does not patentably distinguish claim 126 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 126 corresponds to the proposed Count.

Claim 127 of the Present Application

Claim 127 depends from claim 121 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, V128, H133, N188, A209 and/or M197 in *B. licheniformis*. The '385 patent specification cites and describes PCT Publication No. WO95/10603 as follows:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52]

and WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the specific substitutions Ala-111-Thr, His, 133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

This limitation does not patentably distinguish claim 127 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 127 corresponds to the proposed Count.

Claim 128 of the Present Application

Claim 128 of the present application is an independent claim which corresponds substantially to the proposed Count. The proposed Count and claim 128 call for a variant of a parent alpha-amylase. Claim 128 specifically identifies the parent alpha-amylase as having the amino acid sequence of SEQ ID Nos: 2, 4, 6, or 13 of the present application or an amino acid sequence with a specific homology thereto as determined by a specific computer program. SEQ ID No: 2 of the present application corresponds to the amino acid sequence of *B. licheniformis* alpha-amylase. Specification, p. 4, ll. 21-22. SEQ ID No: 4 of the present application corresponds to the amino acid sequence of *B. amyloliquefaciens* alpha-amylase. Specification, p. 4, ll. 23-24. SEQ ID No. 6 of the present application corresponds to the amino acid sequence of *B. stearothermophilus* alpha-amylase. Specification, p. 4, ll. 25-26. SEQ ID No: 13 of the present application corresponds to the amino acid sequence of an alpha-amylase having a N-terminus from *B. amyloliquefaciens* alpha-amylase and a C-terminus from *B. licheniformis* alpha-amylase. Response to Notice to Comply with Sequence Rules and Amendment mailed January 27, 2000, Specification (amended), p.7, l. 19. Each is a parent alpha-amylase as in the proposed Count.

Each of the amino acid positions identified in claim 128 of the present application is an amino acid position of the proposed Count.

Therefore, the proposed Count and claim 128 of the present application are directed to the same patentable invention.

Claim 129 of the Present Application

Claim 129 depends from claim 128 and further specifies that the alpha-amylase is produced by *Bacillus*. The '385 patent specification acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that "α-Amylases are produced by a wide variety of microorganisms including Bacillus...." Exh. 1, 1:23-24.

This limitation does not patentably distinguish claim 129 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 129 corresponds to the proposed Count.

Claim 130 of the Present Application

Claim 130 depends from claim 129 and further specifies that the alpha-amylase is produced by *B. licheniformis, B. amyloliquefaciens,* or *B. stearothermophilus*. The '385 patent acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that most commercial amylases were produced by *B. licheniformis, B. amyloliquefaciens, B. subtilis*, or *B. stearothermophilus*. Exh. 1, 1:25-28.

This limitation does not patentably distinguish claim 130 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 130 corresponds to the proposed Count.

Claim 131 of the Present Application

Claim 131 depends from claim 128 and further specifies a detergent which comprises the alpha-amylase of claim 128. The '385 patent specification, in the "BACKGROUND OF THE INVENTION" cites PCT Publication No. WO94/10603 as disclosing *B. licheniformis* alpha-amylase variants which have improved laundry or dishwashing performance. Exh. 1, 1:47-52. The '385 patent further states, in the BACKGROUND OF THE INVENTION, that:

> α-Amylases are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing, α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 131 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 131 corresponds to the proposed Count.

Claim 132 of the Present Application

Claim 132 depends from claim 128 and further specifies a starch liquefaction composition which comprises the alpha-amylase of claim 128. The '385 patent specification, in the "BACKGROUND OF THE INVENTION", cites PCT Publication No. WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the

> specific substitutions Ala-111-Thr, His-133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

Again, the '385 patent further states that:

> α-Amylase are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing. α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 132 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 132 corresponds to the proposed Count.

Claim 133 of the Present Application

Claim 133 depends from claim 128 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, N188, A209 and/or M197 in *B. licheniformis*. The '385 patent specification cites and describes PCT Publication No. WO95/10603 as follows:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52].

This limitation does not patentably distinguish claim 133 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 133 corresponds to the proposed Count.

Claim 134 of the Present Application

Claim 134 depends from claim 128 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, V128, H133, N188, A209 and/or M197 in *B. licheniformis*. The '385 patent specification cites and describes PCT Publication No. WO95/10603 as follows:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52]

and WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the specific substitutions Ala-111-Thr, His, 133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

This limitation does not patentably distinguish claim 134 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 134 corresponds to the proposed Count.

Claim 135 of the Present Application

Claim 135 depends from claim 128 and further specifies that the alpha-amylase is modified by substituting an amino acid at a position corresponding to one or more of G301, H405 and/or H406 in *B. licheniformis*. These amino acid positions are members of the group of amino acid positions specified in claim 128 of the present application. Therefore, the proposed Count and claim 135 of the present application are directed to the same patentable invention.

This limitation does not patentably distinguish claim 135 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 135 corresponds to the proposed Count.

Claim 136 of the Present Application

Claim 136 of the present application is an independent claim which is identical to claim 128, except that the amino acid positions specified are Q298, G299, G301, Y302, L307, F343, H405, H406, D407, I428, D430, and G475 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 136 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 136 of the present application are directed to the same patentable invention.

Claim 137 of the Present Application

Claim 137 depends from claim 136 and further specifies that the alpha-amylase is produced by *Bacillus*. The '385 patent specification acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that "α-Amylases are produced by a wide variety of microorganisms including Bacillus...." Exh. 1, 1:23-24.

This limitation does not patentably distinguish claim 137 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 137 corresponds to the proposed Count.

Claim 138 of the Present Application

Claim 138 depends from claim 137 and further specifies that the alpha-amylase is produced by *B. licheniformis, B. amyloliquefaciens,* or *B. stearothermophilus*. The '385 patent acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that most commercial amylases were produced by *B. licheniformis, B. amyloliquefaciens, B. subtilis*, or *B. stearothermophilus*. Exh. 1, 1:25-28.

This limitation does not patentably distinguish claim 138 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 138 corresponds to the proposed Count.

Claim 139 of the Present Application

Claim 139 depends from claim 136 and further specifies a detergent which comprises the alpha-amylase of claim 136. The '385 patent specification, in the "BACKGROUND OF THE INVENTION" cites PCT Publication No. WO94/10603 as disclosing *B. licheniformis* alpha-amylase variants which have improved laundry or dishwashing performance. Exh. 1, 1:47-52. The '385 patent further states, in the BACKGROUND OF THE INVENTION, that:

> α-Amylases are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing, α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 139 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 139 corresponds to the proposed Count.

Claim 140 of the Present Application

Claim 140 depends from claim 136 and further specifies a starch liquefaction composition which comprises the alpha-amylase of claim 136. The '385 patent specification, in the "BACKGROUND OF THE INVENTION", cites PCT Publication No. WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the specific substitutions Ala-111-Thr, His-133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

Again, the '385 patent further states that:

> α-Amylase are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing. α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 140 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 140 corresponds to the proposed Count.

Claim 141 of the '385 Patent

Claim 141 depends from claim 136 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, N188, A209 and/or M197 in *B. licheniformis*. The '385 patent specification cites and describes PCT Publication No. WO95/10603 as follows:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52].

This limitation does not patentably distinguish claim 141 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 141 corresponds to the proposed Count.

Claim 142 of the Present Application

Claim 142 depends from claim 136 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, V128, H133, N188, A209 and/or M197 in *B. licheniformis*. The '385 patent specification cites and describes PCT Publication No. WO95/10603 as follows:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52]

and WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are

approached by genetically engineering the α-amylase to include the specific substitutions Ala-111-Thr, His, 133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

This limitation does not patentably distinguish claim 142 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 142 corresponds to the proposed Count.

Claim 143 of the Present Application

Claim 143 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is Q298 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 143 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 143 of the present application are directed to the same patentable invention.

Claim 144 of the Present Application

Claim 144 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is G299 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 144 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 144 of the present application are directed to the same patentable invention.

Claim 145 of the Present Application

Claim 145 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is G301 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 145 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 145 of the present application are directed to the same patentable invention.

Claim 146 of the Present Application

Claim 146 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is Y302 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 146 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 146 of the present application are directed to the same patentable invention.

Claim 147 of the Present Application

Claim 147 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is L307 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 147 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 147 of the present application are directed to the same patentable invention.

Claim 148 of the Present Application

Claim 148 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is F343 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 148 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 148 of the present application are directed to the same patentable invention.

Claim 149 of the Present Application

Claim 149 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is F403 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 149 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 149 of the present application are directed to the same patentable invention.

Claim 150 of the Present Application

Claim 150 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is H405 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 150 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 150 of the present application are directed to the same patentable invention.

Claim 151 of the Present Application

Claim 151 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is H406 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 151 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 151 of the present application are directed to the same patentable invention.

Claim 152 of the Present Application

Claim 152 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is D407 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 152 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 152 of the present application are directed to the same patentable invention.

Claim 153 of the Present Application

Claim 153 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is L427 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 153 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 153 of the present application are directed to the same patentable invention.

Claim 154 of the Present Application

Claim 154 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is L428 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 154 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 154 of the present application are directed to the same patentable invention.

Claim 155 of the Present Application

Claim 155 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is D430 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 155 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 155 of the present application are directed to the same patentable invention.

Claim 156 of the Present Application

Claim 156 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is G433 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 156 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 156 of the present application are directed to the same patentable invention.

Claim 157 of the Present Application

Claim 157 of the present application is an independent claim which is identical to claim 128, except that the amino acid position specified is G475 in *B. licheniformis*. For the reasons explained above with respect to claim 128, claim 157 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 157 of the present application are directed to the same patentable invention.

Claim 158 of the Present Application

Claim 158 of the present application is an independent claim which corresponds substantially to the proposed Count. The proposed Count and claim 158 call for a variant of a parent alpha-amylase. Claim 158 specifically identifies the parent alpha-amylase as having the amino acid sequence of SEQ ID Nos: 2, 4, 6, or 13 of the present application. SEQ ID No: 2 corresponds to the amino acid sequence of *B. licheniformis* alpha-amylase. Specification, p. 4, ll. 21-22. SEQ ID No: 4 corresponds to the amino acid sequence of *B. amyloliquefaciens* alpha-amylase. Specification, p. 4, ll. 23-24. SEQ ID No. 6 corresponds to the amino acid sequence of *B. stearothermophilus* alpha-amylase. Specification, p. 4, ll. 25-26. SEQ ID No: 13 corresponds to the amino acid sequence of an alpha-amylase having a N-terminus from *B. amyloliquefaciens* alpha-amylase and a C-terminus from *B. licheniformis* alpha-amylase. Sequence Rules and Amendment mailed January 27, 2000, Specification (amended), p.7, l. 19. Each is a parent alpha- amylase as in the proposed Count.

Each of the positions identified in claim 158 of the present application is a position of the proposed Count.

Therefore, the proposed Count and claim 158 of the present application are directed to the same patentable invention.

Claim 159 of the Present Application

Claim 159 depends from claim 158 and further specifies that the alpha-amylase is produced by *Bacillus*. The '385 patent specification acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that "α-Amylases are produced by a wide variety of microorganisms including Bacillus...." Exh. 1, 1:23-24.

This limitation does not patentably distinguish claim 159 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 159 corresponds to the proposed Count.

Claim 160 of the Present Application

Claim 160 depends from claim 159 and further specifies that the alpha-amylase is produced by *B. licheniformis, B. amyloliquefaciens,* or *B. stearothermophilus*. The '385 patent acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that most commercial amylases were produced by *B. licheniformis, B. amyloliquefaciens, B. subtilis*, or *B. stearothermophilus*. Exh. 1, 1:25-28.

This limitation does not patentably distinguish claim 160 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 160 corresponds to the proposed Count.

Claim 161 of the Present Application

Claim 161 depends from claim 158 and further specifies a detergent which comprises the alpha-amylase of claim 158. The '385 patent specification, in the "BACKGROUND OF THE INVENTION" cites PCT Publication No. WO94/10603 as disclosing *B. licheniformis* alpha-amylase variants which have improved laundry or dishwashing performance. Exh. 1, 1:47-52. The '385 patent further states, in the BACKGROUND OF THE INVENTION, that:

> α-Amylases are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing, α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 161 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 161 corresponds to the proposed Count.

Claim 162 of the Present Application

Claim 162 depends from claim 158 and further specifies a starch liquefaction composition which comprises the alpha-amylase of claim 158. The '385 patent specification, in the "BACKGROUND OF THE INVENTION", cites PCT Publication No. WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the

specific substitutions Ala-111-Thr, His-133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

Again, the '385 patent further states that:

> α-Amylase are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing. α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 162 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 162 corresponds to the proposed Count.

Claim 163 of the Present Application

Claim 163 depends from claim 158 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, N188, A209 and/or M197 in *B. licheniformis*. The '385 patent specification cites and describes PCT Publication No. WO95/10603 as follows:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52].

This limitation does not patentably distinguish claim 163 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 163 corresponds to the proposed Count.

Claim 164 of the Present Application

Claim 164 depends from claim 158 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, V128, H133, N188, A209 and/or M197 in *B. licheniformis*. The '385 patent specification cites and describes PCT Publication No. WO95/10603 as follows:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52]

and WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the specific substitutions Ala-111-Thr, His, 133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

This limitation does not patentably distinguish claim 164 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 164 corresponds to the proposed Count.

Claim 165 of the Present Application

Claim 165 depends from claim 158 and further specifies that the alpha-amylase is modified by substituting an amino acid at a position corresponding to one or more of G301, H405 and/or K436 in *B. licheniformis*. These amino acid positions are members of the group of amino acid positions specified in claim 158 of the present application. Therefore, the proposed Count and claim 165 of the present application are directed to the same patentable invention.

Claim 166 of the Present Application

Claim 166 of the present application is an independent claim which is identical to claim 158, except that the amino acid positions specified are Q298, G299, G301, Y302, L307, F343, H405, H406, D407, I428, D430, and G475 in *B. licheniformis*. For the reasons explained above with respect to claim 158, claim 166 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 166 of the present application are directed to the same patentable invention.

Claim 167 of the Present Application

Claim 167 depends from claim 166 and further specifies that the alpha-amylase is produced by *Bacillus*. The '385 patent specification acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that "α-Amylases are produced by a wide variety of microorganisms including Bacillus...." Exh. 1, 1:23-24.

This limitation does not patentably distinguish claim 167 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 167 corresponds to the proposed Count.

Claim 168 of the Present Application

Claim 168 depends from claim 167 and further specifies that the alpha-amylase is produced by *B. licheniformis, B. amyloliquefaciens,* or *B. stearothermophilus*. The '385 patent acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that most

commercial amylases were produced by *B. licheniformis, B. amyloliquefaciens, B. subtilis*, or *B. stearothermophilus*. Exh. 1, 1:25-28.

This limitation does not patentably distinguish claim 168 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 168 corresponds to the proposed Count.

Claim 169 of the Present Application

Claim 169 depends from claim 166 and further specifies a detergent which comprises the alpha-amylase of claim 166. The '385 patent specification, in the "BACKGROUND OF THE INVENTION" cites PCT Publication No. WO94/10603 as disclosing *B. licheniformis* alpha-amylase variants which have improved laundry or dishwashing performance. Exh. 1, 1:47-52. The '385 patent further states, in the BACKGROUND OF THE INVENTION, that:

> α-Amylases are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing, α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 169 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 169 corresponds to the proposed Count.

Claim 170 of the Present Application

Claim 170 depends from claim 166 and further specifies a starch liquefaction composition which comprises the alpha-amylase of claim 166. The '385 patent specification, in the "BACKGROUND OF THE INVENTION", cites PCT Publication No. WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the specific substitutions Ala-111-Thr, His-133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

Again, the '385 patent further states that:

> α-Amylase are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing. α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 170 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 170 corresponds to the proposed Count.

Claim 171 of the '385 Patent

Claim 171 depends from claim 166 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, N188, A209 and/or M197 in

B. licheniformis. The '385 patent specification cites and describes PCT Publication No. WO95/10603 as follows:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52].

This limitation does not patentably distinguish claim 171 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 171 corresponds to the proposed Count.

Claim 172 of the Present Application

Claim 172 depends from claim 166 and adds that the alpha-amylase further comprises a substitution or deletion at one or more residues equivalent to M15, V128, H133, N188, A209 and/or M197 in *B. licheniformis*. The '385 patent specification cites and describes PCT Publication No. WO95/10603 as follows:

> In PCT Publication No. WO95/10603, α-amylase variants are disclosed which have improved laundry or dishwashing performance and comprise a mutation other than a single mutation at position M197 in *Bacillus licheniformis* α-amylase. [Exh. 1, 1:48-52]

and WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the specific substitutions Ala-111-Thr, His, 133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

This limitation does not patentably distinguish claim 172 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 172 corresponds to the proposed Count.

Claim 173 of the Present Application

Claim 173 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is Q298 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 173 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 173 of the present application are directed to the same patentable invention.

Claim 174 of the Present Application

Claim 174 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is G299 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 174 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 174 of the present application are directed to the same patentable invention.

Claim 175 of the Present Application

Claim 175 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is G301 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 175 corresponds substantially to the proposed

Count. Therefore, both the proposed Count and claim 175 of the present application are directed to the same patentable invention.

Claim 176 of the Present Application

Claim 176 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is Y302 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 176 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 146 of the present application are directed to the same patentable invention.

Claim 177 of the Present Application

Claim 177 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is L307 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 177 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 177 of the present application are directed to the same patentable invention.

Claim 178 of the Present Application

Claim 178 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is F343 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 178 corresponds substantially to the proposed

Count. Therefore, both the proposed Count and claim 178 of the present application are directed to the same patentable invention.

Claim 179 of the Present Application

Claim 179 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is F403 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 179 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 179 of the present application are directed to the same patentable invention.

Claim 180 of the Present Application

Claim 180 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is H405 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 180 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 180 of the present application are directed to the same patentable invention.

Claim 181 of the Present Application

Claim 181 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is H406 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 181 corresponds substantially to the proposed

Count. Therefore, both the proposed Count and claim 181 of the present application are directed to the same patentable invention.

Claim 182 of the Present Application

Claim 182 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is D407 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 182 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 152 of the present application are directed to the same patentable invention.

Claim 183 of the Present Application

Claim 183 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is L427 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 183 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 183 of the present application are directed to the same patentable invention.

Claim 184 of the Present Application

Claim 184 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is L428 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 184 corresponds substantially to the proposed

Count. Therefore, both the proposed Count and claim 184 of the present application are directed to the same patentable invention.

Claim 185 of the Present Application

Claim 185 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is D430 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 185 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 185 of the present application are directed to the same patentable invention.

Claim 186 of the Present Application

Claim 186 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is G433 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 186 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 186 of the present application are directed to the same patentable invention.

Claim 187 of the Present Application

Claim 187 of the present application is an independent claim which is identical to claim 166, except that the amino acid position specified is G475 in *B. licheniformis*. For the reasons explained above with respect to claim 166, claim 187 corresponds substantially to the proposed

Count. Therefore, both the proposed Count and claim 187 of the present application are directed to the same patentable invention.

Claim 192 of the Present Application

Claim 192 of the present application is an independent claim which corresponds substantially to the proposed Count. The proposed Count and claim 192 call for a variant of a parent alpha-amylase. Claim 192 specifically identifies the parent alpha-amylase as having the amino acid sequence of SEQ ID No: 2 of the present application. SEQ ID No: 2 corresponds to the amino acid sequence of *B. licheniformis* alpha-amylase. Specification, p. 4, ll. 21-22.

The positions identified in claim 192 of the present application encompass two of the positions of the proposed Count. Furthermore, the '385 patent specification explains that:

> The segments of the α-amylase polypeptide chain which comprise the CalB binding site include residues 290-309, 339-347, 402-411, 426-436 and 472-477. These polypeptide segments comprise the CalB binding site. Accordingly, regiospecific random mutations in these regions would be expected to yield variants that modulate the stability of α-amylase via modulation of the affinity of calcium at this site [Eh. 1, 9:42-49].

Therefore, the proposed Count and claim 192 of the present application are directed to the same patentable invention.

Claim 193 of the Present Application

Claim 193 of the present application is an independent claim which corresponds substantially to the proposed Count. Claim 193 is identical to the proposed Count except that the amino acid positions specified are Q298, G299, G301, Y302, L307, F343, F403, H405, H406, D407,

L427, I428, D430, G433, and G475 in *B. licheniformis*. Therefore, both the proposed Count and claim 193 of the present application are directed to the same patentable invention.

Claim 194 of the Present Application

Claim 194 of the present application depends form claim 193 and specifies amino acid position Q298 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 194 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 194 of the present application are directed to the same patentable invention.

Claim 195 of the Present Application

Claim 195 of the present application depends from claim 193 and specifies amino acid position G299 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 195 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 195 of the present application are directed to the same patentable invention.

Claim 196 of the Present Application

Claim 196 of the present application depends from claim 193 and specifies amino acid position G301 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 196 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 196 of the present application are directed to the same patentable invention.

Claim 197 of the Present Application

Claim 197 of the present application depends from claim 193 and specifies amino acid position Y302 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 197 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 197 of the present application are directed to the same patentable invention.

Claim 198 of the Present Application

Claim 198 of the present application depends from claim 193 and specifies amino acid position L307 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 198 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 198 of the present application are directed to the same patentable invention.

Claim 199 of the Present Application

Claim 199 of the present application depends from claim 193 and specifies amino acid position F343 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 199 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 199 of the present application are directed to the same patentable invention.

Claim 200 of the Present Application

Claim 200 of the present application depends from claim 193 and specifies amino acid position F403 in *B. licheniformis*. For the reasons explained above with respect to claim 193,

claim 200 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 200 of the present application are directed to the same patentable invention.

Claim 201 of the Present Application

Claim 201 of the present application depends from claim 193 and specifies amino acid position H405 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 201 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 201 of the present application are directed to the same patentable invention.

Claim 202 of the Present Application

Claim 202 of the present application depends from claim 193 and specifies amino acid position H406 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 202 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 202 of the present application are directed to the same patentable invention.

Claim 203 of the Present Application

Claim 203 of the present application depends from claim 193 and specifies amino acid position D407 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 203 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 203 of the present application are directed to the same patentable invention.

Claim 204 of the Present Application

Claim 204 of the present application depends from claim 193 and specifies amino acid position G427 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 204 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 204 of the present application are directed to the same patentable invention.

Claim 205 of the Present Application

Claim 205 of the present application depends from claim 193 and specifies amino acid position I428 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 205 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 205 of the present application are directed to the same patentable invention.

Claim 206 of the Present Application

Claim 206 of the present application depends from claim 193 and specifies amino acid position D430 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 206 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 206 of the present application are directed to the same patentable invention.

Claim 207 of the Present Application

Claim 207 of the present application depends from claim 193 and specifies amino acid position G433 in *B. licheniformis*. For the reasons explained above with respect to claim 193,

claim 207 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 207 of the present application are directed to the same patentable invention.

Claim 208 of the Present Application

Claim 208 of the present application depends from claim 193 and specifies amino acid position G475 in *B. licheniformis*. For the reasons explained above with respect to claim 193, claim 208 corresponds substantially to the proposed Count. Therefore, both the proposed Count and claim 208 of the present application are directed to the same patentable invention.

Claim 209 of the Present Application

Claim 209 depends from claim 193 and further specifies that the alpha-amylase is produced by *Bacillus*. The '385 patent specification acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that "α-Amylases are produced by a wide variety of microorganisms including Bacillus...." Exh. 1, 1:23-24.

This limitation does not patentably distinguish claim 209 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 209 corresponds to the proposed Count.

Claim 210 of the Present Application

Claim 210 depends from claim 193 and further specifies that the alpha-amylase is produced by *B. licheniformis, B. amyloliquefaciens,* or *B. stearothermophilus*. The '385 patent acknowledges in the "BACKGROUND OF THE INVENTION" that it was known that most

commercial amylases were produced by *B. licheniformis, B. amyloliquefaciens, B. subtilis*, or *B. stearothermophilus*. Exh. 1, 1:25-28.

This limitation does not patentably distinguish claim 210 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 210 corresponds to the proposed Count.

Claim 211 of the Present Application

Claim 211 depends from claim 193 and further specifies a detergent which comprises the alpha-amylase of claim 193. The '385 patent specification, in the "BACKGROUND OF THE INVENTION" cites PCT Publication No. WO94/10603 as disclosing B. licheniformis alpha-amylase variants which have improved laundry or dishwashing performance. Exh. 1, 1:47-52. The '385 patent further states, in the BACKGROUND OF THE INVENTION, that:

> α-Amylases are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing, α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis or Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 211 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 211 corresponds to the proposed Count.

Claim 212 of the Present Application

Claim 212 depends from claim 193 and further specifies a starch liquefaction composition which comprises the alpha-amylase of claim 193. The '385 patent specification, in the "BACKGROUND OF THE INVENTION", cites PCT Publication No. WO91/00353 as disclosing that:

> the performance characteristics and problems associated with liquefaction with wild-type *Bacillus licheniformis* α-amylase are approached by genetically engineering the α-amylase to include the specific substitutions Ala-111-Thr, His-133-Tyr and/or Thr-149-Ile. [Exh. 1, 1:62-67].

Again, the '385 patent further states that:

> α-Amylase are of considerable commercial value, being used in the initial stages (liquefaction) of starch processing: in alcohol production; as cleaning agents in detergent matrices; and in the textile industry for starch desizing. α-Amylases are produced by a wide variety of microorganisms including Bacillus and Aspergillus, with most commercial amylases being produced from bacterial sources such as *Bacillus licheniformis, Bacillus amyloliquefaciens, Bacillus subtilis* or *Bacillus stearothermophilus*. [Exh. 1, 1:19-27].

This limitation does not patentably distinguish claim 212 of the present application from the prior art, the invention disclosed in the present application, or the proposed Count. Accordingly, claim 212 corresponds to the proposed Count.

Claim 213 of the Present Application

Claim 213 of the present application is an independent claim which corresponds substantially to the proposed Count. Claim 2134 is identical to the proposed Count except that the amino acid positions specified are Q298, G299, G301, Y302, L307, H405, H406, D407, I428, D430,

and G475 in *B. licheniformis*. Therefore, both the proposed Count and claim 213 of the present application are directed to the same patentable invention.

VII. Application Pursuant to 37 C.F.R. §1.607(a)(5) of the Claims Identified as Corresponding to the Proposed Count and not Previously in the Application to the Disclosure of the Application

Attached as Exhibit 3 is a claim chart applying claims 193-213 to the original disclosure to demonstrate full support for those claims. This claim chart was submitted as Appendix 1 to the Supplemental Preliminary Amendment filed concurrently herewith which added claims 193-213 to the present application.

VIII. Explanation of How the Requirements of 35 U.S.C. §135(b) Are Met by Claims of the Present Application which Were Not Present in the Application until More than One Year after the Issue Date of U.S. Patent No. 5,763,385

Claims 70-112 were added in compliance with 35 U.S.C. §135(b) to the present application by the Preliminary Amendment mailed June 8, 1999, less than one year after the issue date of the '385. *See* M.P.E.P. §2307, "Applicant Requests Interference With a Patent - COMPLIANCE WITH 35 U.S.C. §135(b)". These claims were for the same or substantially the same subject matter as at least one of the claims of the '385 patent. 35 U.S.C. §135(b). Certain of claims 70-112 were canceled and claims 113-192 were added by the Supplemental Preliminary Amendment filed April 19, 2000. Certain of claims 113-192 are canceled and claims 193-213 are added by the Supplemental Preliminary Amendment filed concurrently herewith. However, all of the remaining claims in the present application added subsequent to June 8, 1999, are directed to the

same or substantially the same subject matter as the claims that were pending in the present application on June 9, 1999, the one year anniversary date of the issuance of the '385 patent, and to the same or substantially the same subject matter as at least one of the claims of the '385 patent. Particularly:

Pending claims 113, 121, 128, 136, 158, 166, 192, and 193 of the present application correspond substantially to claim 70 (presented June 8, 1999) of the present application;

Pending claims 114, 122, 129, 137, 159, 167, and 202 of the present application correspond substantially to claim 71 (presented June 8, 1999) of the present application;

Pending claims 115, 123, 130, 138, 160, 168, and 210 of the present application correspond substantially to claim 72 (presented June 8, 1999) of the present application;

Pending claims 116, 124, 131, 139, 161, 169, and 211 of the present application correspond substantially to claim 73 (presented June 8, 1999) of the present application;

Pending claims 117, 125, 132, 140, 162, 170, and 212 of the present application correspond substantially to claim 74 (presented June 8, 1999) of the present application;

Pending claims 118, 119, 126, 127, 133, 134, 141, 142, 163, 164, 171, and 172 of the present application correspond substantially to claim 75 (presented June 8, 1999) of the present application;

Pending claims 120, 135, and 165 of the present application correspond substantially to claim 76 (presented June 8, 1999) of the present application;

Pending claims 143, 173, and 194 of the present application correspond substantially to claim 77 (presented June 8, 1999) of the present application;

Pending claims 144, 174, and 195 of the present application correspond substantially to claim 78 (presented June 8, 1999) of the present application;

Pending claims 145, 175, and 196 of the present application correspond substantially to claim 79 (presented June 8, 1999) of the present application;

Pending claims 146, 176, and 197 of the present application correspond substantially to claim 80 (presented June 8, 1999) of the present application;

Pending claims 147, 177, and 198 of the present application correspond substantially to claim 81 (presented June 8, 1999) of the present application;

Pending claims 148, 178, and 199 of the present application correspond substantially to claim 84 (presented June 8, 1999) of the present application;

Pending claims 149, 179, and 200 of the present application correspond substantially to claim 85 (presented June 8, 1999) of the present application;

Pending claims 150, 180, and 201 of the present application correspond substantially to claim 86 (presented June 8, 1999) of the present application;

Pending claims 151, 181, and 202 of the present application correspond substantially to claim 87 (presented June 8, 1999) of the present application;

Pending claims 152, 182, and 203 of the present application correspond substantially to claim 88 (presented June 8, 1999) of the present application;

Pending claims 153, 183, and 204 of the present application correspond substantially to claim 90 (presented June 8, 1999) of the present application;

Pending claims 154, 184, and 205 of the present application correspond substantially to claim 91 (presented June 8, 1999) of the present application;

Pending claims 155, 185, and 206 of the present application correspond substantially to claim 92 (presented June 8, 1999) of the present application;

Pending claims 156, 186, and 207 of the present application correspond substantially to claim 93 (presented June 8, 1999) of the present application;

Pending claims 157, 187, and 208 of the present application correspond substantially to claim 97 (presented June 8, 1999) of the present application; and

Pending claims 147, 177, and 198 of the present application correspond substantially to claim 81 (presented June 8, 1999) of the present application.

Therefore, the present application and the present Request are in compliance with 35 U.S.C. §135(b).

IX. Identification Pursuant to 37 C.F.R. §1.607(c) of Application Claims which Correspond Substantially to Claims of U.S. Patent No. 5,763,385

Applicants submit that:

Claims 113, 121, 128, 136, 158, 166, 192, 193, and 213 of the present application correspond substantially to claim 1 of the '385 patent;

Claims 11, 122, 129, 137, 159, 167, and 209 of the present application correspond substantially to claim 2 of the '385 patent;

Claims 115, 123, 130, 138, 160, 168, and 210 of the present application correspond substantially to claim 3 of the '385 patent;

Claims 116, 124, 131, 139, 161, 169, and 211 of the present application correspond substantially to claim 4 of the '385 patent;

Claims 117, 125, 132, 140, 162, 170, and 212 of the present application correspond substantially to claim 5 of the '385 patent;

Claims 118, 119, 126, 127, 133, 134, 141, 142, 163, 164, 171, and 172 of the present application correspond substantially to claim 6 of the '385 patent;

Claims 120, 135, and 165 of the present application correspond substantially to claim 7 of the '385 patent;

Claims 77, 143, 173, and 194 of the present application correspond substantially to claim 8 of the '385 patent;

Claims 78, 144, 174, and 195 of the present application correspond substantially to claim 9 of the '385 patent;

Claims 79, 145, 175, and 196 of the present application correspond substantially to claim 10 of the '385 patent;

Claims 80, 146, 176, and 197 of the present application correspond substantially to claim 11 of the '385 patent;

Claims 81, 147, 177 and 198 of the present application correspond substantially to claim 12 of the '385 patent;

Claims 84, 148, 178, and 199 of the present application correspond substantially to claim 15 of the '385 patent;

Claims 85, 149, 179, and 200 of the present application correspond substantially to claim 16 of the '385 patent;

Claims 86, 150, 180, and 201 of the present application correspond substantially to claim 17 of the '385 patent;

Claims 87, 151, 181, and 202 of the present application correspond substantially to claim 18 of the '385 patent;

Claims 88, 152, 182, and 203 of the present application correspond substantially to claim 19 of the '385 patent;

Claims 90, 153, 183, and 204 of the present application correspond substantially to claim 21 of the '385 patent;

Claims 91, 154, 184, and 205 of the present application correspond substantially to claim 22 of the '385 patent;

Claims 92, 155, 185, and 206 of the present application correspond substantially to claim 23 of the '385 patent;

Claims 93, 156, 186, and 207 of the present application correspond substantially to claim 24 of the '385 patent; and

Claims 97, 157, 187, and 208 of the present application correspond substantially to claim 28 of the '385 patent for the reasons and exceptions noted above.

X. Statement Obviating Showing under 37 C.F.R. §1.608

The present application is a continuation application of U.S. S. N. 08/683,838, filed July 18, 1996, now issued as U.S. Patent No. 6,022,724; which was a continuation-in-part application of U.S.S.N. 08/600,908, filed February 13, 1996, now issued as U.S. Patent No. 5,989,169; which was a continuation application of PCT application no. PCT/DK96/00057, filed February 5, 1996; which claimed priority from Danish patent application nos. DK0128/95, filed February 3, 1995, DK1192/95, filed October 23, 1995, and DK1256/95, filed November 10, 1995.

Therefore, the present application is entitled to an effective filing date of at least as early as February 3, 1995.

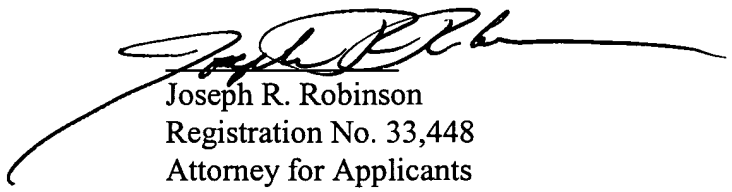
The application that issued as the '385 patent was filed on May 14, 1996. Therefore, the earliest effective filing date that might be accorded the '385 patent is May 14, 1996.

The present application has an effective filing date prior to the effective fling date of the '385 patent. Accordingly, a showing under 37 C.F.R. §1.608 is unnecessary.

XI. Conclusion

In view of the foregoing, applicants submit that there is interfering subject matter between the present application and U.S. Patent No. 5,763,385 and request that an interference be declared.

Respectfully submitted,



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